

are at the minimum if the method described is followed. Doctor Taussig's fear of atrophic radiodermatitis is unwarranted with this method except in desperate cases and, if the area of dermatitis is small, it can be treated surgically. Small areas quite often heal without a scar. Ectropion following treatment of lesions of the lower lid by properly controlled radiation is most unusual. It is as unfair to compare the poor results and injuries that follow the improper use of radiation with those following skillful surgical treatment as it is to compare the deep, puckered scars, ectropions, and other deformities so often seen after unskillful surgical treatment with those obtained by properly applied irradiation. I do not see why the use of radiation should preclude biopsy, and if omitted the radiologist or dermatologist should be criticized instead of the method. It is true that cartilage heals slowly after heavy radiation, but the physician must weigh the advantage or disadvantage of each method as applied to that particular case. I have treated many ears by radiation when the cartilage was involved with excellent results, but there have also been instances where I have chosen the cautery. I want to emphasize that I do not limit myself to radiation, but choose the method which in that particular case will first cure the cancer and, second, but second only, produce the least deformity. The reason for using the time-honored method of curettage and desiccation followed by radiation, described by Doctor Wilhelm, has always puzzled me. Why, if the radiation is given to destroy the cancer left after the preliminary treatment, should it not be used in the first place? The argument that cells at the short depth involved in these lesions would not be reached unless the upper ones were removed does not apply if the proper effective wavelength and dose is used. This is well known to all radiologists. I want to remind the discussers before closing that this method is not mine alone, nor did I originate it. It is used throughout the world, and reports from many cancer centers show results such as I have described.

In closing let me again repeat that I hold no brief for any particular method, that I am not limited to radiation in treating these superficial malignancies, and that I use radiation in the majority of these cases because, first, its percentage of cures is as high as by any other and, second, that as a rule, except in very small lesions, the cosmetic results are superior.

UNDULANT FEVER*

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DISCUSSION by K. F. Meyer, Ph. D., San Francisco; C. W. Bonyng, M. D., Los Angeles; J. C. Geiger, M. D., San Francisco.

FOR centuries an obscure fever has been known to exist about the shores of the Mediterranean Sea. Hippocrates records observations leading us to believe that undulant fever existed in his time. He describes protracted fevers, lasting for many months, some with rhythmically recurring pyrexial waves that easily suggest the term "undulant." We cannot prove that the disease thus pictured is the same as the one that now engages our attention, for it was only in 1859 that Marston gave the full and minute description that makes identification possible. This keen observer, stationed at Malta, had the opportunity to study many instances of a disease prevailing on the Island, characterized by irregular relapses and

remissions of fever, splenic enlargement, and a low mortality; and, by differentiating it from typhoid and other prevalent fevers there, clearly established it as a distinct entity.

Veale, in 1879, also differentiated it clearly from malarial fever. In 1886, Bruce isolated an organism from the spleen of a patient dying of the disease, which was later corroborated by Hughes in 1891, and the name *micrococcus melitensis* was given to it.

BRITISH COMMISSION AT MALTA

Because of the tremendous inroads made by this fever upon the personnel of the army and navy stationed at Malta, the British Government appointed a commission to study the disease. This commission made elaborate investigations from 1904 to 1907, and reported that the fever, known as Malta Fever, was due to a septicemia caused by the *micrococcus melitensis*, and that 10 to 15 per cent of the goats on the Island of Malta had this organism in their milk. Following this report, goat's milk for the troops on the Island was prohibited, and the cases of Malta Fever dropped from 750 cases in 1905 to none in 1907, and has practically disappeared from the British garrison since this date.

BACILLUS ABORTUS

The discovery by Bang of the *bacillus abortus* as a causative agent of contagious abortion in cattle was an event of equal importance in a seemingly entirely distinct field. This disease is prevalent in every part of the world where cattle are raised, and has always been a serious economic problem.

Evans, working in the Hygienic Laboratory in Washington, demonstrated the identity, or at least a very close similarity between the organism of contagious abortion and the organism of Malta Fever. They can be differentiated only by agglutination absorption tests.

However, it was not until the report of Keefer that human infection from this organism was proved. It is now well established that the abortus variety of *Brucella melitensis* may infect human beings and produce a disease clinically indistinguishable from undulant fever of the Mediterranean.

BRUCELLA MELITENSIS AND BRUCELLA ABORTUS

Many series of experiments have now been completed by various workers, and have proved that *Brucella melitensis*, the cause of Malta Fever, and *Brucella abortus*, which is the cause of endemic abortion of cattle and hogs, are closely related organisms.

Evans and Meyer classified this group of organisms, and have succeeded in growing many strains which have a varied pathogenicity to human beings. In order to correlate the knowledge of this disease, Meyer and Shaw proposed that the entire group be named *Brucella* in honor of Doctor Bruce, who isolated *melitensis* in 1886.

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This name has been generally adopted, and these organisms are known in the literature as *Brucella melitensis* and *Brucella abortus*.

INCIDENCE OF UNDULANT FEVER

The instance and distribution of undulant fever in continental United States is widespread, and it can hardly be doubted that it occurs in every state in the union. However, it is noteworthy:

1. That there are large areas in the country from which no cases have been reported.
2. That there is a permanent local area of goat infection in Texas, which has existed for at least forty years.
3. That the extent of infection in those states from which the disease is reported varies greatly.
4. That in heavily infected states, such as Iowa or New York, the disease is widely disseminated and occurs both in the country districts and in large cities.
5. That, although epidemics are uncommon, we notice widespread outbreaks in Iowa, New York and Michigan.

Foci connected with the goat-raising industry have been known for many years in certain parts of Arizona and New Mexico, and it is to be expected that undulant fever of caprine origin will be found wherever goat raising is a prominent industry. It is clear that in most infected states the disease is entirely independent of the goat raising industry, and we may place in the category of proven cases those occupational ones of porcine origin, which occur among slaughter house employees, and laboratory infections among bacteriologists.

From an epidemiological viewpoint, it is those cases which are now quite generally assumed to be due to cow's milk infected with the *Brucella abortus* type of organism which should claim our attention.

As has been stated, there are two groups of cases concerning the origin of which no doubt exists:

1. The group associated with the goat raising industry;
2. The occupational groups of porcine or laboratory origin.

It has been generally assumed that cases not of these origins are due to the transmission, through cow's milk, of the *abortus* type of *Brucella*, originally described by Bang of Copenhagen, and referred to in older literature as the *Brucella abortus* of Bang. Decisive proof, however, that the milk of cattle suffering from contagious abortion can transmit undulant fever to man is, in many instances, lacking. Some of these facts are as follows:

1. Contagious abortion among cattle is a disease which is widespread throughout many parts of this country.
2. Undulant fever is least common among those members of the community who drink the largest amount of milk, namely children.

3. Actual experiments of feeding healthy individuals with milk known to be infected with bovine *Brucella abortus* have been made with negative results.

4. It is easy to prove that an individual is infected with an organism of the *Brucella* group, but it is much more difficult to decide which particular member of the group is responsible.

PATHOGENICITY OF DIFFERENT TYPES

There is no question as to the pathogenicity of the caprine type. The difficulty lies in distinguishing the bovine from the porcine type. Such evidence as exists at the present time regarding the pathogenicity for man of the bovine or porcine type of *Brucella abortus* suggests very strongly that the porcine type is responsible even in those cases which appear to be transmitted by cow's milk. We must conclude that there has not been sufficient study of the origin of undulant fever to enable us to reach a definite decision as to the source of the infecting organism, although existing evidence points towards the porcine type rather than the bovine.

This does not eliminate cow's milk as a source of infection, for the reason that cattle, as well as man, may be infected by the porcine type of *Brucella abortus*. There are other factors which must certainly be taken into consideration, such as the possibility that *Brucella abortus* of the bovine type may, in certain localities, have taken on increased pathogenicity.

A STUDY BY THE U. S. PUBLIC HEALTH SERVICE

A detailed study by the United States Public Health Service of 484 cases reported in 1930 by Hazeltine showed that the ratio of infections according to sex was three males to one female. It was also noted that there was a comparatively low incidence in young children, which rapidly increased in adolescence and early adult life. Generally speaking, only one case occurred in a household. Three distinct epidemiological groups were noted:

1. Those having little or no contact with livestock or carcasses.
2. Those having contact with livestock, and carcasses in the meat packing industry.
3. Those having contact with livestock on the farm.

Hazeltine divides these cases into three groups:

1. The milk group, 198 cases. . . .
2. The meat group consisted of forty packing house employees, two butchers, one worker in a rendering plant, and one employee in a plant manufacturing hog cholera serum.
3. The farm group, 193 cases. . . .

DIFFERENTIATION OF VARIETIES

While it is desirable that as much light as possible be thrown upon the differentiation of varieties, it is a matter of small importance from the standpoint of the patient. The unfortunate

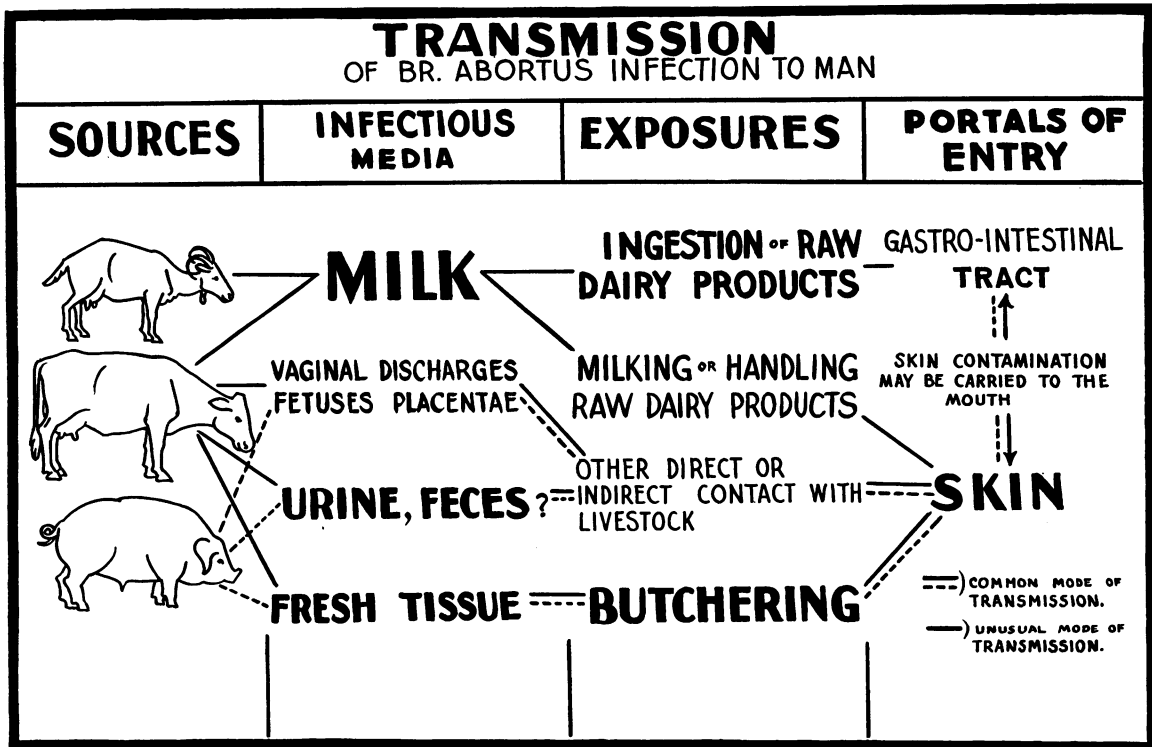


Fig. 1. Etiological factors of undulant fever (Hardy).

individual finds himself ill with a continued disabling fever, no matter what strain is associated with his case. All varieties of *Brucella* give an agglutination reaction against a common antigen, and when symptoms are produced, all cases appear clinically identical. For the present we should consider the *Brucella* genus rather than the species or variety.

All three varieties of *Brucella* have been isolated from cattle. Apparently the Suis, or porcine variety, is able to infect nearly all species of domestic animals, and the possibility of infection coming from unusual animal sources should not be overlooked in the epidemiological investigations.

Up to the present, transmission from one human being to another by contact appears very infrequently, if at all. The finding of *Brucella* in the stools of patients by Amos and Poston warns us that such transmission may be possible.

Madsen reports that in Denmark seven out of eight pregnant women aborted, and in two of these *Brucella abortus* was found in the placenta.

SYMPTOMS

The key which opens the door of diagnosis is suspicion. Doctors have always met with obscure fevers. We should be suspicious that any unexplained fever, especially if it assumes an undulating type, is undulant fever, even in cases of single attacks of fever of apparently brief duration.

The fever, which is the outstanding manifestation and which gives the disease its name, is remarkable. It has a peculiar, irregular curve consisting of intermittent waves, or undulations, of a distinctly remittent type, lasting from three months, the average, to two years. The undula-

tions may be separated by apyrexical periods of varying length, so that relapses are common.

Hughes describes four types:

1. The intermittent type, with insidious onset, and mild course, with temperature rarely exceeding 100 degrees to 101 degrees. The symptoms are vague, the most prominent of which are headache, insomnia, anorexia, possibly epigastric tenderness, muscle or joint pains, and sweats. The course is consistently mild, and rarely do any more striking features present themselves.

2. The undulant type, the more common type, and in many respects, the most typical of what the name undulant fever implies. There is an undulating type of fever in which the elevations are higher, with headache, anorexia, insomnia, pains in the head, back and limbs, epigastric tenderness, and obstinate constipation. Here, also, the profuse sweats, so commonly seen, occur with greatest frequency.

3. The malignant type occurs with sudden onset, runs a stormy course and is rapidly fatal. Fortunately, this type is uncommon. Fever reaches high proportions, with rapid development of typhoid state, coma, heart failure, and death.

4. The ambulant type in which the fever is so slight as to be unaccompanied by any discomfort, and even unrecognized until sought for by examination of the blood for specific agglutinins.

The incubation period is now generally agreed to be approximately two weeks, although it has been noted that laboratory and experimental infections occur in a much shorter time, usually in from five to seven days.

The onset of undulant fever may be sudden or insidious. During this period, which varies widely,

Infections of the Genito-Urinary Tract.—These may be complications of a *Brucella* infection, and hence an agglutination should be made for undulant fever in cases where pus is found in the urine, associated with frequency and painful micturition, as this may be one of the uncommon features of *Brucella* infection.

PROGNOSIS

In infections that can be attributed to the abortus variety of *Brucella melitensis*, it is safe to give a fair prognosis to this type of case, as there has been a case fatality of less than three per cent. However, our prognosis must be somewhat guarded when our infections are known to be of the caprine variety of *Brucella melitensis*, and also somewhat guarded in that type of infections that are known to be of the porcine variety. The individual is ill in varying degrees, from a few weeks to two years.

TREATMENT

There is no record of any type of known therapy which is specific for undulant fever. In the literature one finds many different specifics recommended, usually because of the uneventful recovery of a few treated cases. . . .

Because of this, it is now possible better to evaluate the different therapeutic procedures recommended. Those procedures of proven value, and of first importance, are rest, light diet, adequate fluids, and appropriate measures for the alleviation of prominent symptoms. Exercise in convalescence should be followed closely by temperature recordings, and so modified that elevations of fever above 100 degrees Fahrenheit are prevented.

There are many therapeutic measures of unproved value, and the one most commonly recommended is the use of specific vaccine. While this measure has not been used in a large number of cases, it has been observed that rapid recovery follows administration of the vaccine in cases of undulant fever, but it also has been noted that in other cases infections continued unmodified by the same treatment. . . .

ECONOMICS OF UNDULANT FEVER

Undulant fever has begun to play a very prominent part in the economics of our country. It behooves us to determine in the near future definitely the question of its etiology. Because of the close relationship between the animal diseases and the human infections, it is assumed that undulant fever is an animal-borne disease.

The economics of such a disease, which disables an individual for a period of time from a few months to two years, is far-reaching. Again we have the economics as related to industry, and the production and sale of raw milk, and the inspection and elimination from our herds of all animals giving a positive test for undulant fever. The fires of the unending war between the advocates of pasteurized and raw milk are caused to burn more brightly, because of the assumption that the disease is distributed by the use of raw milk.

1930 Wilshire Boulevard.

DISCUSSION

K. F. MEYER, Ph.D. (Hooper Foundation for Medical Research, University of California).—In order to appreciate the importance of the undulant fever problem, certain statistical data referring to the State of California may be of interest. During the period January, 1927 to January, 1934, five hundred and ninety-one cases of undulant fever have been reported. Although widely distributed throughout the State, the ten southern counties form a solid block reporting four hundred and six cases, or 68.69 per cent of the total number observed within the boundaries of the State. Los Angeles City is represented with 31 per cent of the total. The histories of these cases are by no means complete, but it is noteworthy that in 50 per cent of the established infections no other possible source than raw cow's milk is mentioned. Unfortunately, many of the clinical cases were seen late in the course of their illness, and consequently blood cultures were either not attempted or, when made, proved unsuccessful. In order to elucidate the many unknown pathways of a *Brucella* infection in an urban population, it is absolutely imperative that cultures be secured. Valuable information may thus be obtained as to the types of the organisms which caused the infections. With increasing frequency, the "suis" type of porcine origin has been isolated from employees of meat-packing establishments who contracted the disease in the course of their occupational duties. Equally important are the latent infections, particularly in the rural communities and among those who have contact with infected animals. The newer diagnostic methods—allergic and phagocytic index tests—materially aid in the recognition of these cases. Since the majority of undulant fever cases are diagnosed serologically, it appears imperative that the physicians appreciate that the evaluation and interpretation of these tests are by no means a simple matter. The following criteria are herewith recommended:

1. A titer of 1:80 or less, in the absence of clinical symptoms, is probably indicative of a past clinical or subclinical infection.

2. A titer of 1:100 or over, in the absence of clinical signs of disease, in all probability indicates a latent infection which may not necessarily be accompanied by disease. Such titers are not uncommon in occupational or professional groups which come in contact with *Brucella* organisms and contract their infections through the skin.

3. A titer of 1:100 or over, in the presence of fever or other fairly typical symptoms of the disease, may be considered as diagnostic of active infection with an organism of the *Brucella* group. In persons other than veterinarians, packing-house employees, farm workers or those consuming large quantities of raw milk from non-tested herds, this interpretation may hold true in the majority of instances. Exceptions, however, do occur, and blood cultures, together with the demonstration of a rise and gradual fall of titer in from three to twelve months, must then confirm the clinical diagnosis.

4. A titer of 1:20 to 1:100 in the presence of clinically diagnosed undulant fever may be interpreted as diagnostic of active infection. Patients with positive blood cultures, without having developed agglutinins above 1:80, have been observed.

5. A complete absence of agglutinins from a patient's serum, in the presence of a positive blood culture, has been observed on one or two occasions.

The diagnosis of undulant fever demands the closest cooperation between the clinician and the serologist. Until this prerequisite has been fulfilled, the statistics on this disease remain uncertain.



C. W. BONYNGE, M. D. (1930 Wilshire Boulevard, Los Angeles).—Doctor Ruddock has presented a most complete treatise on undulant fever, and in its discussion I would only bring out a few facts regarding its epidemiology.

In spite of a vast amount of experimental study with both animals and human volunteers, it is freely admitted that little is known as to the mode of transmission of this disease. This is true both as regards its dissemination among animals and its passage from them to man.

When it became known that the organism of infectious abortion of cattle was pathogenic for man, ingestion of raw milk and its by-products was considered the greatest source of human Brucellosis. However, those best qualified to express an opinion consider that but one out of every three infections originates from this source. While milk from infected animals is undeniably an important factor in the etiology of undulant fever, consideration of this disease from the standpoint of preventive medicine must be undertaken in a broad-minded manner.

Efficient pasteurization of milk is entirely effective *per se*, but in no way influences the continuous spread of the disease among the dairy herds and to humans in contact with them.

It is becoming more and more evident that we must look to veterinary science for the final solution of the problem, and I feel the medical profession hardly appreciates the contributions this group have made to human medicine in this and in other diseases.

Control of Bang's disease among the vast reservoir which the farm animals of our country constitute, is uppermost in the minds of all veterinarians, and its importance recognized by the Federal Government. While this measure still presents certain difficulties, its success has been demonstrated by the fact that milk may be maintained free of organisms.

I hardly need to bring to your attention that the first and soundest principle of preventive medicine is the eradication of the reservoir from which springs an infectious disease.

Public opinion is proving a powerful factor in forcing the dairyman to adopt abortion control, and I feel the medical profession should support the project by educating the layman to take an interest in the status of his milk supply, even though it be pasteurized.

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J. C. GEIGER, M. D. (Director of Public Health, San Francisco).—The significance of the problem of undulant fever to the clinician and to the public health worker has been stressed by many writers. Doctor Ruddock's contribution, however, is timely, and brings out in a very definite manner many of the facts that have been ascertained and which should be made available to the medical profession. There is, of course, another reason for doing this in that the practicing physician may be stimulated to scrutinize more carefully such cases as may resemble the disease, especially as to all possible sources of infection. At the very beginning it may be necessary to call attention to the statement of Evans; for in this disease, as in perhaps no other, the laboratory may offer decided help to the careful and thoughtful clinician. This statement is to the effect that there is no disease in which the physician is more dependent upon laboratory findings for correct diagnoses. The symptoms are various, indefinite and suggestive of other disease, particularly typhoid fever, malaria, tuberculosis, and rheumatism. To these diseases may now be also added focal infection, sinusitis, appendicitis, and tularemia. Moreover, some cases have been diagnosed as acute anterior poliomyelitis. In many diseases certain symptoms often can be spoken of as classical. Undulant fever has not this distinctive characteristic at this moment. The available evidence indicates that the causative organisms are of three general types, and usually classified as to hosts. The variety known as *Brucella melitensis* ordinarily prefers the goat; *Brucella abortus* (Bang) ordinarily prefers the cow; and *Brucella abortus*, variety porcine, ordinarily prefers the hog. Any one of these may cause undulant fever in man.

The epidemiologic evidence is far from being definite, complete or conclusive. There is no doubt that

raw milk, whether it be from goat or cows, offers undisputable chances for infection, provided the herds supplying them are shedding the organism in sufficient amounts and are of sufficient virulence. Therefore, pasteurization of milk products is an essential control and preventive measure. The low index of the disease in children, and the present statistical superiority of the disease in males, especially in rural sections, has been used as a basis for assuming that many cases may be due to contact with infected animals.

The incubation period is considered around fourteen to twenty-one days, more likely near the latter. The chronicity of the illness, however, may preclude against obtaining this accurately. Raw milk from goats or cows should not be directly blamed unless laboratory data are obtained as the shedding of organisms in the milk, or the extent of the infection in the herd determined by agglutination tests or by history of recent abortions in the herd, or the recent use of live organism abortus vaccines, or by direct inoculation of guinea-pigs of centrifugized specimens of pooled milk samples. Any assumption that infected raw milk is the causative factor should be carefully scrutinized and all other possible avenues closed. It is probable, however, that continuous ingestion of smaller numbers of abortus organisms of all types will lead to mild or unrecognized cases.

Contact infection is considered by many investigators as the most likely source of infection. By contact is meant the laboratory worker with abortus strains or infected animals; the farm worker; the goat herder; cow hand or swine attendant who might handle infected material, particularly in the abortion period; the workers in slaughterhouses; and the veterinarian. Direct contact from human to humans is unknown, and exceedingly doubtful. The investigator, however, should not be unmindful of abortion in women, particularly in rural communities. Undulant fever is reportable, but as a rule no special precautions or quarantine procedures are necessary in handling the human case. There must be appreciated, however, that the British Commission repeatedly isolated organisms from the urine of cases of true *Brucella melitensis* infections.

There is evidence, however, that the first two strains, *Brucella melitensis*, caprine strain (goats), and *Brucella abortus suis*, porcine strain (hogs), are more invasive than *Brucella abortus bovis*, bovine strain (cattle).

While it has been shown in a number of instances that invasion by the first two strains (caprine and porcine) has followed contact with infected animals, this route of infection is less common in cases due to the third strain (bovine). Furthermore, in most cases due to the presence of the bovine strain, the source of infection has probably been ingestion of infected milk, milk products, or raw infected meat or meat products.

It may be assumed, therefore, on the basis of available information at this time, that the bovine type is less invasive in that it fails to induce noteworthy symptoms. It is possible, also, that invasion by this strain may immunize against the more virulent strains of caprine or porcine types.

On the other hand, it should be remembered that cattle may be affected by the caprine and the porcine strains, as well as by the bovine strains, and that the names are applied to the strains for the reason that their usual occurrence is in the animal referred to. In other words, the porcine strain affecting the cow could, through contact, be transmitted to man because of its highly invasive characteristics; but, on the other hand, the bovine strain affecting the hog might be less invasive and therefore give rise either to no invasion or to so mild an invasion that it would not be identified as Brucellosis.

The controversial state of the entire question, while less complex than it was a few years ago, is such that there are still many points indefinitely determined, especially to the health official.